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Evaluation of Real-world Data for Breast-MRI BI-RADS IV Lesions

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Abstract. *Background/Aim: Magnetic resonance imaging (MRI) is an important diagnostic tool in the detection of breast cancer. The Breast Center of the municipal Hospital Holweide, Cologne, annually cares for and treats patients with changes in the breast. A special problem is posed by Breast Imaging-Reporting and Data System (BI-RADS) 4 lesions. If a BI-RADS 4 finding is present, is a vacuum biopsy indicated in every case or, if there is already an indication for surgery due to other findings, can the corresponding finding be removed openly without histological clarification? We require real world data regarding the actual in-center likelihood of a BIRADS 4 lesion to be DCIS (Ductal carcinoma in situ) or invasive disease. Patients and Methods: This is a retrospective study of 1,641 patients who received MRI examination in the radiological department of the municipal hospital Holweide in 2012 and 2013. Each BI-RADS 4 finding (or higher) classified by MRI was compared with the final histological result. Results: 347 MRIs showed BI-RADS 4 findings or higher and 280 (80.7%) cases showed benign histology. In 67 (19.3%) cases, histology showed DCIS or invasive carcinoma. Conclusion: BI-RADS 4 lesions have a low probability of malignancy based on real-world data from this center. If there is already an indication for surgery due to other lesions, the patient can also be offered a simultaneous open biopsy in the context of the already initiated surgical treatment. Each center should know the sensitivity and specificity of the MRI imaging performed and counsel patients based on that.*

Magnetic resonance imaging (MRI) was developed in the 1980s and is now an important diagnostic tool in modern medicine. The first use of MRI with contrast agents for the diagnosis of breast cancer was reported in 1986 (1). Due to its high sensitivity for breast cancer, MRI has assumed important roles in the detection, differential diagnosis, and monitoring of breast cancer. For breast MRIs usually an additional contrast agent, gadolinium, is used. Crucial to MRI-based breast cancer diagnosis is the concept of tumor angiogenesis or neovascularity. Tumor-associated blood vessels have increased permeability. This results in gadolinium release in the corresponding tissue within the first one to two minutes after uptake. That tumor-typical pattern of rapid accumulation and washout helps distinguish breast cancer from benign lesions (2).

In the detection of breast cancer, MRI is characterized above all by a high sensitivity of 88-100%, which has been demonstrated in several studies (3-6). Regarding sensitivity, breast MRI is superior to mammography, breast sonography, and physical examination (7, 8). However, the lower specificity appears to be disadvantageous. Peters *et al*. were able to demonstrate specificity of 72% for breast cancer in a meta-analysis including 44 studies (9). The Breast Imaging-Reporting and Data System (BI-RADS) classification to standardize MRI findings was introduced by the American College of Radiology (ACR) for breast MRIs in 2003 and its

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latest update was published in 2019. If mammography, digital tomosynthesis, and sonography reveal suspicious or unclear findings, *i.e.,* corresponding to a BI-RADS 4, further clarification using MRI may be considered. More indications for MRI are the diagnosis of occult primary breast cancers, determination of disease extent in newly diagnosed breast cancer patients, the assessment of silicone implant integrity, documentation of response to neoadjuvant chemotherapy and diagnosis of recurrence. Furthermore, MRI is an extremely important pillar especially in the care of high-risk patients. In 2005, a multimodality surveillance program was initiated by the German Consortium for Hereditary Breast and Ovarian Cancer (GC-HBOC) screening of high-risk patients, which included a minimum one-year breast MRI examination. Bick *et al*. were able to show significant benefit for patients participating in the program. Within 10 years, 221 cases of breast cancer were diagnosed through the program. In 61 (30.8%) cases, a diagnosis was made solely by MRI (High-risk breast cancer surveillance with MRI: 10-year experience from the German consortium for hereditary breast and ovarian cancer).

The breast center of the municipal Hospital Holweide, Cologne, annually cares for and treats many patients with changes in the glandular body of the breast. Approximately 600 new cases of breast cancer are diagnosed and subsequently treated each year. This also means that a correspondingly large number of patients with unclear and most likely benign diseases undergo clarifying diagnostics. A special problem is posed by BI-RADS 4 lesions, which raise the question of how to proceed with further clarification. If a corresponding lesion is seen on MRI, there is basically the option of a vacuum biopsy *versus* an open specimen collection. If carcinoma is suspected, histological confirmation should be performed first in order to plan further therapy accordingly. The most common mode of histological evaluation is an MRI biopsy. This is time consuming and expensive. If a BI-RADS 4 finding is present, is a vacuum biopsy indicated in every case or, if there is already an indication for surgery due to other findings, can the corresponding finding be removed openly without histological clarification? To answer this question, we, therefore, require real world data regarding the actual in-center likelihood of a BIRADS 4 lesion to be DCIS or invasive disease. This needs to be firmly established over the course of several years for each breast cancer center before individual management of the lesion may be suggested to the patients.

Patients and Methods

This is a retrospective study. In total 1,641 requests for breast MRIs were analyzed. All patients received the MRI examination in the radiological department of the municipal hospital Holweide, Cologne in the years 2012 and 2013. The MRI used in our study is the Philips Gyroscan ACS-NT 1.5T (Philips, Amsterdam, the Netherlands).

Each BI-RADS 4 finding (or higher) classified using MRI was compared with the final histological result. In case there was no histological confirmation possible, or one examination yielded simultaneously multiple results, such as DCIS and carcinoma, the case was excluded. Additionally, patients were excluded when MRI was impaired *e.g.,* due to contrast intolerance or excessive weight of patients.

Table I. *Histopathological results of BI-RADS 4 or higher lesions.*

	Number of cases
Mammary carcinoma	47 (13.5%)
DCIS	20 (5.8%)
Mastopathy	112 (32.3%)
Fibroadenoma	33 (0.5%)
Papilloma	19 (5.5%)
Fibrosis	60 (17.3%)
Usual ductal hyperplasia	16 (4.6%)
Lobular intraepithelial neoplasia	15 (4.3%)
Others[1]	25 (7.2%)

[1]Other findings included scar tissue, Siliconoma, necrosis, galactostasis, lymph nodes and atrophic lipomatosis.

Results

In total, 1,641 requests for breast MRIs were analyzed. One hundred ten patients were excluded from further analysis. Reasons for this were excessive weight or abdominal girth of the patient, no-show of the patient for histological confirmation, contrast intolerance, or patient refusal. A total of 1,183 findings were classified as BI-RADS 3 or lower whereas 347 MRIs showed BI-RADS 4 findings or higher. Thirty-eight examinations were excluded since there was no histological result available. 280 (80.7%) cases showed benign histology as shown in Table I. Benign findings comprised 112 cases of mastopathy, 33 of fibroadenoma, 19 of papilloma, 60 of fibrosis, 16 of usual duct hyperplasia, 15 of lobular intraepithelial neoplasia and 25 cases of other findings such as siliconoma, necrosis, galactostasis, lymph nodes, and atrophic lipomatosis. In 67 (19.3%) cases, histology showed DCIS or invasive carcinoma (Figure 1).

The median age of the patients was 51.51 years. Table II shows the tumor biology of those cases with MRI findings classified as BI-RADS 4 or higher and histologically proven DCIS or invasive carcinoma. Of the 67 patients with a BI-RADS 4 or higher, 47 had invasive carcinoma. In 7 patients, DCIS and breast cancer were found to be present simultaneously. Thus, 40 patients with carcinoma (11.76%) and 20 patients (5.88%) with DCIS were included in the final evaluation. Twenty patients with an invasive carcinoma

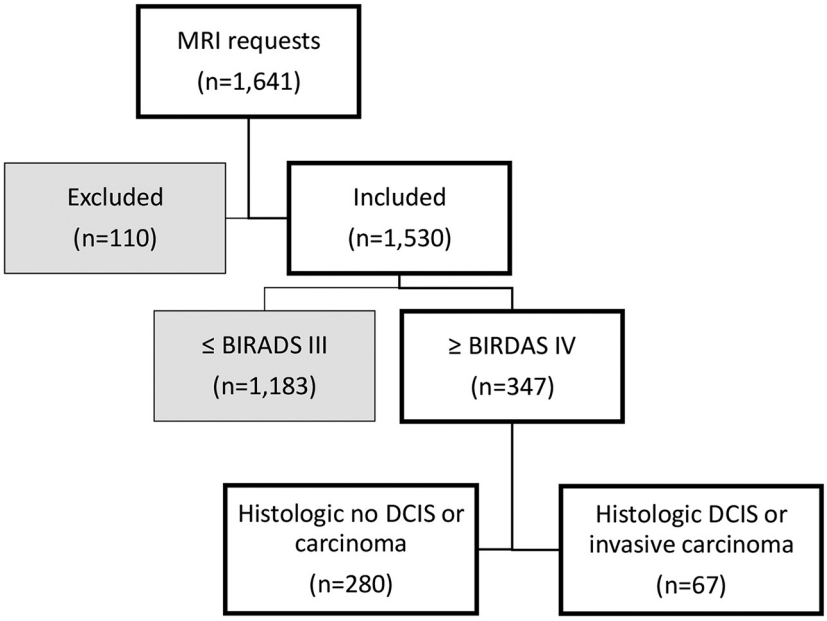

Figure 1. *Overview of all magnetic resonance imaging (MRI) cases. A total of 110 patients were excluded from further analysis. Reasons for this were excessive weight or abdominal girth of the patient, no-show of the patient for histological confirmation, contrast intolerance, or patient refusal. In total, 1,183 findings were classified as BI-RADS 3 or lower whereas 347 MRIs showed BI-RADS 4 findings or higher.*

were initially describe as BI-RADS 4 in MRI examination. In our study the percentage of invasive carcinoma with BI-RADS 4 lesions was 8.26%.

Discussion

This is a retrospective study to assess the effectiveness of breast MRI for BI-RADS 4 lesions based on real-world data provided by 1,641 breast-MRIs performed in 2012 and 2013. BI-RADS 4 lesions do not meet the criteria for malignancy, but still, appear suspicious enough to warrant a biopsy. Based on its definition, the probability of malignancy is between 2% and 95%. In addition to the morphologic appearance of the lesion, the contrast image is crucial for the BI-RADS classification. A benign lesion is characterized by slow and uniform contrast uptake (type 1 curve), whereas malignancy-susceptible lesions show initial strong contrast uptake followed by rapid washout (type 3 curve). Moderate to strong contrast uptake followed by a plateau (type 2 curve) may be a sign for both benign and malignant tumor (10). In 2013, the American College of Radiology released a newer BI-RADS 4 classification. BI-RADS 4 is now divided into category 4a (risk of malignancy 2-10%), category 4b (risk of malignancy 10-50%), and category 4c (risk of malignancy 50-95%) (11).

Our study consists of real-world data of 1641 breast MRIs recorded in 2012 and 2013. It, therefore, does not include the previously mentioned sub-classification. In our analysis, we were able to show that the specificity of breast MRI for BI-RADS-4 or higher lesions is 19.3%. This is a significantly lower specificity than reported in a 2017 meta-analysis by Bennani-Bait *et al*. (12). In 20 studies, a sensitivity of 92% (86-96%) *versus* a specificity of 82% (74-88%) for BIRADS 4 findings was described here. However, only the data in the presence of microcalcification were evaluated. In our study, the MRI images were evaluated independently of the presence of previous findings. Nevertheless, our analysis shows that its comparatively low specificity is in favor of a high sensitivity.

MRI is an important and indispensable tool in the diagnosis and treatment planning of breast cancer. Diagnosis based on MRI findings alone, however, causes overtreatment

Table II. *Tumor biology of correctly classified BIRADS IV findings in magnetic resonance imaging.*

		Number of cases
Estrogen-receptor[1]	Positive	46 (78.0%)
	Negative	13 (22.0%)
Progesteron-receptor[1]	Positive	49 (83.1%)
	Negative	10 (17.0%)
HER2- status[2]	Positive	13 (25.5%)
	Negative	38 (74.5%)

[1]For one patient no tumor biology was available. [2]For nine patients no HER2-status was documented.

in over 80% cases. Pettit *et al*. found in 2009 that when the decision for surgery is based only on MRI findings leads to an increased risk of mastectomy in breast cancer patients (13). As our data attest, breast MRI offers its greatest utility in the multidimensional diagnostic workup, particularly in conjunction with sonographic, tomographic, and clinical assessment. In the case of unclear findings, corresponding to a BI-RADS 4 lesion, MRI has a high sensitivity, which is superior to sonographic and clinical diagnosis, but has only a low specificity.

The current German guideline on the diagnosis and treatment of breast cancer recommends histological clarification by vacuum or fine-needle biopsy in the case of unclear findings. This is based on a review analysis from 2010, which evaluated 9 studies and found comparable sensitivity and specificity between vacuum or fine needle biopsy and open biopsy, but with a lower complication rate of the core needle procedures (14). In addition, a definitive histologic workup even in cases of most likely benign findings such as BI-RADS 3 or BI-RADS 41 is in accordance with the wishes of most patients (15). Although vacuum biopsy is a safe method with comparatively few complications, it is associated with increased pain and a slightly increased risk of bleeding (16, 17). In addition, the pain is a trigger for strong stress of the patients during the examination (18). Our study shows that due to the low finding rates of carcinoma in BI-RADS 4 lesions, open biopsy is an option without prior histological clarification if surgery is already indicated.

Conclusion

Findings of BI-RADS 4 lesions should always be clarified by histological confirmation if possible. Our study showed that BI-RADS 4 lesions have a low probability of malignancy based on real-world data from our center. On the basis of our study, if there is already an indication for surgery due to other lesions, the patient can also be offered a simultaneous open biopsy in the context of the already initiated surgical treatment. However, appropriate counseling of the patient can only be provided if the sensitivity and specificity of the MRI examination performed at the center are known, as these may differ from center to center.

Conflicts of Interest

All Authors declare that there are no conflicts of interest regarding this study.

Authors' Contributions

CE and JH designed the study. All Authors contributed to data collection and analysis. JH and CE wrote the article. All Authors revised and approved the final form. CE was the supervisor.

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